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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,694	03/14/2001	Anthony J. Kinney	BB1432 US NA	3560

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/12/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,694	KINNEY ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7 and 91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7 and 91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-3, 5-7, and 91 are pending.

2. Applicant's election without traverse of Group I, claims 1-3, 5-7, and 91 in Paper No. 13 is acknowledged.

Claims 4, and 8-90 have been canceled.

Claim 91 has been added.

Claim 7 has been amended.

3. Claims 1-3, 5-7, and 91 are examined in the present office action.

Claim Objections

4. Claims 5 and 6 are objected to for being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 5-7, and 91 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 3, it is unclear how a construct can lower Soybean vacuolar protein P34 content. Does the construct physically lower the protein content, or is the expression of a nucleic acid that is comprising the construct responsible for lowering the Soybean vacuolar protein P34

content. Applicant needs to explicitly state by what mean the construct is lowering the Soybean vacuolar protein P34 content.

In claims 1 and 3, the recitation "Gly m Bd 30K nucleic acid fragment" is unclear. Does Applicant mean a fragment of Gly m Bd 30K encoding nucleic acid or does Applicant mean a nucleic acid fragment that encodes a Gly m Bd 30K protein?

In claims 1 and 3, the metes and bounds of "substantially" have not been defined. It is unclear to what degree said nucleic acid fragment corresponds to SEQ ID NO:1.

In claims 1 and 3, the metes and bounds of "functionally equivalent subfragment" cannot be determined since Applicant has not defined said function.

In claims 1 and 3, how is a fragment different from a subfragment? Does a subfragment necessarily arise from a fragment?

In claim 5, Applicant has not defined "hypoallergenic soybean plant". What makes the plant "hypoallergenic", what is the allergen to which people are allergic?

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 5-7, and 91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a recombinant expression construct comprising an isolated nucleic acid fragment encoding a Gly m Bd 30K protein in which the fragment corresponds substantially to the nucleotide sequence set forth in SEQ ID NO:1 or a functionally equivalent subfragment thereof.

The specification only discloses the nucleic acid sequence of SEQ ID NO:1 encoding a putative Soybean vacuolar protein P34 and does not disclose any specific structural, physical and/or chemical properties for the claimed sequence. Applicants do not present a description of domains that are specific to this particular Soybean vacuolar protein P34 nor domains that are important for its proper function. In addition, Applicants do not disclose the location of the translation start codon as well as the translation stop codon. Given the lack of description, one skilled in the art would not be able to identify sequences with less than 100% sequence identity that still maintained the proper purported activity. The claims recite fragments corresponding substantially to SEQ ID NO:1 or a functionally equivalent subfragment thereof, but Applicant has not disclosed a representative number of species as encompassed by the claims. The claims encompass mutants and allelic variants and thus imply that structural variants exist in nature, yet no structural variant has been disclosed. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known. Thus, there is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine such mutants and allelic variants from other plants and organisms, absent further guidance. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the

claimed invention. (see Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement.

7. Claims 1-3, 5-7, and 91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a recombinant expression construct comprising a nucleic acid fragment that substantially corresponds to SEQ ID NO:1, or a functionally equivalent subfragment thereof, operably linked to a promoter, and a soybean plant comprising said recombinant expression construct.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicants have only presented a nucleic acid sequence of SEQ ID NO:1 which they purport encodes a soybean P34 protein (otherwise referred to in the claims as Gly m Bd 30K or Soybean vacuolar protein P34) (page 5, lines 36-37). Applicants have not disclosed the specific

details as to how to isolate or obtain SEQ ID NO:1 and Applicants have not demonstrated that SEQ ID NO:1 encodes a functional P34 protein, because Applicants have not disclosed the translation start and stop codons, nor have they presented an assay by which one can test the activity of an isolated protein encoded by nucleic acid fragments as claimed. Applicants have also not generated a Soybean plant transformed with SEQ ID NO:1 that produces a plant with reduced expression of the endogenous P34 protein, that supposedly acts as an allergen. Is the expression of the nucleic acid encoding a protein which is responsible for lowering the Gly m Bd 30K content or is the nucleic acid which is expressed from the expression construct responsible for lowering the Gly m Bd 30K content? In addition, Applicants broadly claim "a fragment corresponding substantially to SEQ ID NO:1 or a functionally equivalent subfragment thereof". The recitation encompasses any sequence that comprises additions, deletions or substitutions at any unspecified position, all of which would not be expected to possess the same activity as Applicants' SEQ ID NO:1. The specification also fails to provide guidance for which amino acids of SEQ ID NO:1 can be altered, and which amino acids must not be changed, to maintain activity and substrate specificity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein. Lastly, the specification fails to disclose how a plant transformed with any of the above mentioned sequences will suppress the expression of the endogenous allergenic protein.

Due to the unpredictable nature of plant transformation, one of skill in the art can not reasonably generate transformed plants with a desired phenotype using a specific isolated gene. Levels of transgene expression in plants are generally unpredictable and vary between

independent transformants; this variability is usually explained by differences in transgene copy number and/or integration site (Finnegan and McElroy, 1994. Bio/technology 12: 883-888 pg. 883 2nd paragraph) Eshed et al (2001, Current Biology 11:1251-1260 pg 1255 2nd paragraph) documented the phenotypes of plants transformed with the 35S CaMV promoter fused to the *KANADI1* gene, which is a gene normally expressed in tissues located on the bottom side of young developing leaves. Of the 30 plants that were transformed with the *KANADI1* gene, 23 plants developed only small narrow cotyledons and an arrested meristem, three produced a few radialized leaves and four appeared normal. These results suggest that transforming plants with an endogenously expressed gene in regions of the plant in which it is not normally expressed produces highly unexpected and unpredictable results.

Applicants claim a recombinant expression construct to lower the Soybean vacuolar protein P34 content in soybean plants but they do not reduce to practice a process that achieves their claimed invention. The state-of-the-art teaches the unpredictable nature of silencing specific genes. Bryant (1989, Trends in Biotechnology 7(2):20-21) teaches using antisense to downregulate chalcone synthase did not always produce plants with the desired result. It was not clear why plants were produced with all levels of regulated chalcone synthase, from plants exhibiting suppression to plants exhibiting a wild-type phenotype (page 20, right column, 1st paragraph). Bryant suggests that "position effect" influences transgene expression (page 20, right column, 2nd paragraph). Martienssen (1998, PNAS 95:2021-2026) teaches essential genes cannot be downregulated because suppression would lead to dominant lethal phenotypes that cannot be maintained (page 2021, left column, 2nd paragraph).

Using sequences exhibiting below a 100% sequence identity as compared to a reference sequence produces unpredictable RNA degradation results. Moonan et al (2002, Journal of Virology 76(3):1339-1348) teach " sugarcane plants expressing untranslated viral capsid sequences of *Sorghum mosaic virus* strain SCH, challenged with SrMV viruses of strains SCM and SCI and *Sugarcane mosaic virus* strain, show various levels of virus resistance that correlated with the percentage of sequence identity of the transgenes to the sequence of the challenging virus" (page 1347, 1st paragraph, right column). Therefore, the protection achieved using sequences that exhibited less than 100% sequence identity to the respective viral gene resulted in an inferior viral protection.

Given the state-of-the-art that teaches the unpredictable nature of plant transformation and gene silencing for the reasons stated above; given the lack of guidance and examples of reducing the content of Soybean vacuolar protein P34 using a recombinant expression construct comprising SEQ ID NO:1 or a fragment corresponding substantially to the nucleotide sequence set forth in SEQ ID NO:1 or a functionally equivalent subfragment thereof; and given the breadth of the claims and lack of exemplified sequences, it would require undue experimentation for one skilled in the art to make and/or use the broadly claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 7 and 91 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 7 and 91 are drawn to a seeds of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only two thirds of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Given that there is no indication that there would be any other distinguishable characteristics of the claimed progeny (seeds), it is unclear whether the claimed seeds would be distinguishable from seeds that would occur in nature. See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 76 USPQ 280 (1948), and *In re Bergy , Coats, and Malik* 195 USPQ 344, (CCPA) 1977. The amendment of the claims to recite that the seeds comprise the construct that was introduced into the parent seed would overcome the rejection.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Kawai et al (May 13, 1997, Japanese Patent Number JP409121870A).

The claim is drawn to a recombinant expression construct comprising a nucleic acid fragment that substantially corresponds to SEQ ID NO:1, or a functionally equivalent subfragment. Given the indefiniteness of "substantially" and "functionally equivalent subfragment" as discussed in the 112 2nd arguments above, the Office interprets the term "fragment that substantially corresponds to SEQ ID NO:1" to mean any nucleic acid molecule that shares at least one base pair with the reference sequence.

Kawai et al teach a thiol protease encoding nucleic acid sequence that exhibits 14.4% identity with Applicants SEQ ID NO:1, and for purposes of molecular biology, would be included in a recombinant expression cassette. The claims are drawn to a product and therefore the intended use holds no patentable weight. Since the prior art teaches the product, the product of the prior art would inherently possess the property of lowering the Gly m Bd 30K content of a soybean plant and as such, anticipates the claimed invention. Deleting the terms "fragment that substantially corresponds to SEQ ID NO:1" and "functionally equivalent subfragment thereof" from the claims will obviate the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-3, 5-7 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai et al (May 13, 1997, Japanese Patent Number JP409121870A) as applied to claim 1 above, and further in view of Kinney et al (December, 1997, World Patent Number WO 97/47731, listed in IDS).

The teachings of Kawai et al have been discussed above.

Kawai et al do not teach a recombinant expression construct comprising any of the promoters listed in claims 2 or 3, nor do they teach a transformed soybean plant comprising said recombinant expression construct.

Kinney et al teach recombinant expression constructs comprising the 35S promoter and beta-conglycinin promoters (pages 11-12) operably linked to a heterologous nucleic acid and soybean transformation thereof (pages 16-18).

It would have been prima facie obvious to one skilled in the art at the time the invention was made to transform a soybean plant with the expression construct of Kawai using any of the heterologous promoters of Kinney to express thiol protease in a soybean plant with a reasonable expectation of success. The use of heterologous promoters was well known in the art, as both Kawai and Kinney used heterologous promoters in their expression constructs. Expression in a plant such as a soybean plant, as taught by Kinney, is also well known, and is an alternative expression system with benefits over bacterial expression systems. The resulting soybean plant would inherently be hypoallergenic, as the claims only require the presence of the expression construct to be hypoallergenic. If such is not the case, then the claims should recite additional elements that would render the plant hypoallergenic. Accordingly, the claimed invention is prima facie obvious in view of the prior art.

11. No claims are allowed. SEQ ID NO:1 is deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:1.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, who may be contacted at 308-0196.

Stuart F. Baum Ph.D.

March 5, 2003

PHUONG T. BUI
PRIMARY EXAMINER
3/5/03